

REMARKS

Claims 1-17 and 19-27 are pending and presently under consideration, prior to Amendment. Applicants cancel, without prejudice, previously withdrawn claims 5-17. Applicants reserve the right to prosecute claims of similar or differing scope in this or future applications.

Applicants have amended claims 1 and 27 to improve the clarity of the claims. Claim 1 has been amended to clarify that the method comprises determining both whether the agent inhibits or attenuates hedgehog signaling and whether the agent inhibits or reduces cell proliferation or growth.

Claim 27 has been amended to clarify that the lung cells *are not lung cancer cells*.

Support for Applicants' amendments are found throughout the specification and previously pending claims. No new matter has been entered.

Applicants add new claims 29-31. Support for the subject matter of the newly added claim is found, for example, in paragraph [0167] of the published specification. No new matter has been entered.

Applicants request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action.

Status of Application, Amendments, and/or Claims

Applicants note that Applicants' after-final amendment was entered in full. Applicants thank the Examiner for the detailed explanation provided in the Advisory Action mailed May 12, 2008.

Withdrawn Objections and/or Rejections

Applicants note that the rejection of claim 27 under 35 U.S.C. § 103(a) as allegedly unpatentable over Marigo et al. in view of Bellusci has been withdrawn.

Rejection of Claims 1, 3, 4, 25, and 26 Under 35 U.S.C. § 103(a)

Claims 1, 3, 4, 25, and 26 are rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Marigo *et al.* (US 6,261,786) and Fujita *et al.* (BBRC 238: 658-665, 1997). Applicants traverse this rejection.

Applicants' after-final response detailed why the cited references fail to render the claimed invention obvious, and Applicants maintain the arguments advanced in the after-final response. In response to Applicants' arguments, the Examiner appears to contend that the claims did not actually require two diagnostic steps. Rather, one of skill in the art could inherently evaluate cell proliferation based on determining changes in hedgehog gene expression. Applicants respectfully disagree with the rationale for maintaining the rejection.

As an initial point, Applicants submit that reliance on inherency in an attempt to overcome deficiencies in the teachings of the cited references is inappropriate. Applicants' position is supported by applicable case law. Although inherency is often relevant in the context of anticipation, it is rarely relevant to an assessment of obviousness. See, for example, *Jones v. Hardy*, 727 F.2d 1524 (Fed. Cir. 1984); *In re Adams*, 53 C.C.P.A. 996 (CCPA 1966); *In re Caldwell*, 50 C.C.P.A. 1464 (CCPA 1963). "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." *Application of Spormann*, 53 C.C.P.A. 1375, 363 F.2d 444, 448, 150 U.S.P.Q. (BNA) 449, 452 (1966) (citing *In re Adams*, 356 F.2d 998, 53 CCPA).

Applicants contend that, prior to Amendment, the cited references fail to render the claimed invention obvious. Nevertheless, to expedite prosecution, Applicants have amended claim 1 to improve its clarity. Specifically, Applicants have amended claim 1 to point out that determining the change in each parameter (e.g., cell proliferation and hedgehog signaling) is evaluated relative to a control. Applicants' amendment is believed to clarify, as detailed in Applicants' previous response, that the claimed method is directed to screening assays in which two parameters are evaluated. Applicants' amendment is not in acquiescence to the rejection. Applicants reserve the right to prosecute claims of similar or differing scope.

Pursuant to MPEP 2142, "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)." The

combined teachings of Marigo *et al.* and Fujita *et al.* fail to satisfy these criteria, and thus fail to undermine the patentability of the claimed invention.

Applicants reiterate the factual and legal arguments of record detailing the numerous ways in which the cited references fail to render the claimed invention obvious. Applicants' amendment serves to further clarify the previously articulated distinctions between the claimed invention and the cited art.

The standard for obviousness under 35 U.S.C. §103 asks whether the claimed invention, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made. An obviousness analysis requires the four factual determinations set forth in *Graham v. John Deere*, 148 USPQ 459 (1966). *See also* MPEP § 2141; *KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (2007). The Examiner has the burden of factually supporting any conclusion of obviousness. *See* MPEP § 2142. In the present case, Applicants contend that the claimed invention, taken as a whole, provides screening assays based on determining multiple parameters. This invention is not rendered obvious by the teachings of Marigo *et al.* and Fujita *et al.*

Applicants contend that the combined teachings of Marigo *et al.* and Fujita *et al.* fail to undermine the patentability of the claimed invention. Accordingly, reconsideration and withdrawal of this rejection are requested.

Rejection of Claims 27 and 28 Under 35 U.S.C. § 112, first paragraph (new matter)

Claims 27 and 28 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. This is a new matter rejection. Applicants traverse this rejection.

Applicants contend that claim 27 is amply supported by the specification. The specification supports methods for identifying agents that function to reduce or inhibit proliferation or growth of lung cells. Further, the specification clearly contemplated that the subject screening methods could be conducted using any of a range of cells, including diseased cells (cancerous and other diseased cells), as well as non-diseased cells (e.g., "healthy" cells). Exemplary support can be found, for example, on page 15, lines 12-14; page 15, lines 26-29; page 16, lines 1-4; and page 48, lines 10-20. Thus, contrary to the Examiner's statement, the specification provides broad support for screening methods conducted generally in lung cells,

including diseased (for example, cancerous) and non-diseased (for example, non-cancerous) cells.

Applicants maintain that claim 27, prior to amendment, is both non-obvious in view of the cited art, and is supported by the specification. Nevertheless, to expedite prosecution, Applicants have amended claim 27 (and claims depending therefrom) to clarify that the lung cells used in the claimed method are *not lung cancer cells*. Applicants' amendment is amply supported by the specification, for example, by the above referenced passages.

Applicants' amendment is not in acquiescence to the rejection. Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of the rejection are requested.

Related Applications

Applicants take this opportunity to bring prior, ongoing, and future prosecution in the following co-pending applications to the Examiner's attention: application serial number 09/804,490; application serial number 09/977,864; application serial number 10/652,298; application serial number 09/883,848; application serial number 10/652,686; and application serial number 10/772,090. The Examiner is invited to consider said prosecution in these co-pending applications. The most recent action in application serial number 09/804,490 is a Notice of Allowance mailed April 18, 2008. The most recent action in application serial number 09/977,864 is a reply and Request for Continued Examination mailed June 9, 2008 (responsive to a Final Office Action mailed March 17, 2008). The most recent action in application serial number 10/652,298 is a reply and Request for Continued Examination mailed June 9, 2008 (responsive to a Final Office Action mailed April 4, 2008). The most recent action in application serial number 09/883,848 is a Final Office Action mailed March 3, 2008. The most recent action in application serial number 10/652,686 is a Final Office Action mailed April 30, 2008. The most recent action in application serial number 10/772,090 is a reply and Request for Continued Examination mailed June 23, 2008 (responsive to a Final Office Action mailed January 8, 2008).

The foregoing applications are made of record on the accompanying Information Disclosure Statement.

CONCLUSION

If any clarification of the above response would facilitate prosecution of this application, Applicants respectfully request that the Examiner contact the undersigned at 617-951-7000. Any fee required for timely consideration of this submission may be charged to **Deposit Account No. 18-1945, under Order No. HUIP-P02-032.**

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Respectfully Submitted,



Melissa S. Rones, Ph.D.

Registration No.: 54,408

ROPES & GRAY LLP

One International Place

Boston, Massachusetts 02110-2624

(617) 951-7000

(617) 951-7050 (Fax)

Attorneys/Agents For Applicant